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TITLE: Diagnostic devices and apparatus for
the controlled movement of reagents without
membranes

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INVENTOR-INFORMATION:

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US-CL-CURRENT: 422/58, 422/102 , 422/61 , 422/73 ,
436/165 , 436/177

CLAIMS:

I claim:

1. An assay device comprising:

i. a sample addition reservoir positioned so that one
side of said sample
addition reservoir is adjacent to a sample reaction barrier
(ii);

ii. a sample reaction barrier between said sample
addition reservoir and
said reaction chamber, said barrier having a capillarity
greater than the
capillarity of said reaction chamber, whereby absent an
externally applied
force, fluid flows from the sample reaction barrier to the
reaction chamber
pursuant to capillary force;

iii. a reaction chamber adapted for receiving fluid
from said sample

reaction barrier, said chamber comprising a wall which comprises at least two fingers;

iv. a time gate positioned immediately adjacent to the reaction chamber to receive fluid into said diagnostic element;

v. a diagnostic element capable of immobilizing at least one conjugate in at least one zone; and.

vi. a used reagent reservoir disposed a capillary space away from said diagnostic element, so that fluid flow is directed into said capillary space.

2. Device of claim 1 wherein said diagnostic element further comprises fingers positioned downstream from said zone or zones to prevent fluid from flowing backwards over said zone(s).

3. Device of claim 1 wherein said diagnostic element is comprised of a non-porous surface.

4. An assay device comprising:

i. a sample addition reservoir;

ii. a reaction chamber;

iii. a sample reaction barrier between said sample addition reservoir and said reaction chamber, said sample reaction barrier having a greater capillarity than said reaction chamber, wherein said reaction chamber is adapted to receive fluid flow from said sample reaction barrier;

iv. a wall perpendicular or substantially perpendicular to fluid flow in said sample reaction barrier, said wall located at the interface between said sample reaction barrier and said reaction chamber, said wall comprising grooves

perpendicular or substantially perpendicular to fluid flow in said sample reaction barrier, said grooves having widths of between 0.5 mm to 2 mm wide and 0.1 mm to 1.5 mm in depth, whereby absent an externally applied force, fluid flows from the sample reaction barrier to the reaction chamber pursuant to capillary force;

iv. a time gate for delaying fluid flow from said reaction chamber to a separation element (v), said time gate located between said reaction chamber and said separation element, said time gate comprising at least one hydrophobic surface which is capable of binding at least one component present in said fluid; and whereby the delay of fluid flow is related to the rate of binding of the component to said hydrophobic surface whereby binding of the component to said hydrophobic surface changes said hydrophobic surface into a hydrophilic surface whereby fluid can flow into said separation element;

v. a separation element capable of entrapping, or removing by binding at least one component from said fluid;

vi. a time gate for delaying fluid flow from said separation element to a diagnostic element (vii) so as to maximize desired binding interactions in said diagnostic element, said time gate located between said separation element and said diagnostic element, said time gate comprising at least one hydrophobic surface which is capable of binding at least one component present in said fluid; and whereby the delay of fluid flow is related to the rate of binding of the component to said hydrophobic surface whereby binding of the component to said hydrophobic surface changes said hydrophobic surface into a hydrophilic surface whereby fluid can flow into said diagnostic element

(vii);

vii. a diagnostic element capable of immobilizing at least one conjugate in at least one zone; and,

viii. a used reagent reservoir.

5. Device of claim 4 wherein said means (vi) is a nonporous or porous surface.

6. Device of claim 4 wherein said diagnostic element (viii) is a nonporous or porous surface.

7. Diagnostic assay device comprising:

i. a sample addition reservoir;

ii. a sample reaction barrier between said sample addition reservoir and a reaction chamber (iii), said sample reaction barrier comprising a first capillary;

iii. the reaction chamber, said reaction chamber comprising a second capillary, said second capillary adapted to receive fluid flow from said first capillary, said first capillary having a greater capillarity than said second capillary;

iv. a wall perpendicular or substantially perpendicular to fluid flow in said first capillary, said wall located at the interface between said first capillary and said second capillary, said wall comprising grooves substantially perpendicular to fluid flow in said first capillary, said grooves having widths of between 0.5 mm to 2 mm wide and 0.1 mm to 1.5 mm in depth, whereby absent an externally applied force, fluid flows from the sample reaction barrier to a reaction chamber pursuant to capillary force;

v. a membrane comprising a time gate, said time gate for delaying fluid flow from said membrane to a diagnostic element (vi), said time gate immobilized in said membrane, with said time gate located next to, or a capillary distance from, said diagnostic element, said time gate comprising at least one hydrophobic surface which is capable of binding at least one component present in said fluid; and whereby the delay of fluid flow is related to the rate of binding the component to said hydrophobic surface whereby binding of the component to said hydrophobic surface changes said hydrophobic surface into a hydrophilic surface whereby fluid can flow into said diagnostic element;

vi. a diagnostic element capable of immobilizing at least one conjugate in at least one zone; and,

vii. a used reagent reservoir.

8. An assay device comprising:

i. a sample addition reservoir;

ii. a reaction chamber;

iii. a sample reaction barrier between said sample addition reservoir and said reaction chamber, said sample reaction barrier having a greater capillarity than said reaction chamber, wherein said reaction chamber is adapted to receive fluid flow from said sample reaction barrier;

iv. a wall perpendicular or substantially perpendicular to a fluid flow direction in said sample reaction barrier, said wall located at the interface between said sample reaction barrier and said reaction chamber, said wall comprising grooves perpendicular or substantially perpendicular to the fluid

flow direction in said sample reaction barrier, said grooves having widths of between 0.5 mm to 2 mm wide and 0.1 mm to 1.5 mm in depth, whereby absent an externally applied force, fluid flows from the sample reaction barrier to a reaction chamber pursuant to capillary force; and.

v. a diagnostic element capable of immobilizing at least one conjugate in at least one zone, said diagnostic element fluidly connected to said reaction chamber.

9. The device of claim 8 further comprising a used reagent reservoir, fluidly connected to said diagnostic element.

10. The device of claim 8 wherein the sample addition reservoir comprises a filter element capable of removing particulate matter from a sample.

11. The device of claim 8 further comprising a means for entrapping, or removing by binding, at least one component from a fluid.

12. The device of claim 8 wherein said diagnostic element is a nonporous surface or a porous surface.

13. The device of claim 8 further comprising a time gate that can delay flow of a fluid.

14. The device of claim 13 wherein the time gate is located on a hydrophilic surface between said reaction chamber and said diagnostic element, or on a hydrophobic surface between said reaction chamber and said diagnostic element.

15. The device of claim 13 wherein the time gate is adapted to allow fluid flow from said reaction chamber to said diagnostic element through said time gate by capillary action, surface tension, hydrostatic

pressure or a
combination thereof.

16. The device of claim 13 wherein the time gate is positioned between said reaction chamber and said diagnostic element, wherein the time gate delays fluid flow from said reaction chamber to the diagnostic element, said time gate comprising at least one hydrophobic surface which is capable of binding at least one component present in said fluid; and whereby the delay of fluid flow is related to the rate of binding the component to said hydrophobic surface, whereby binding of the component to the hydrophobic surface changes said hydrophobic surface into a hydrophilic surface whereby fluid can advance.

17. An assay device for detecting at least one target ligand in a fluid sample, the device comprising:

a first capillary region and a second capillary region, said first capillary region having a greater capillarity than said second capillary region; and,

a wall perpendicular or substantially perpendicular to a fluid flow direction in said first capillary region, said wall located at an interface between said first capillary region and said second capillary region, said wall comprising grooves perpendicular or substantially perpendicular to the fluid flow direction in said first capillary region, wherein said grooves are between 0.5 mm to 2 mm wide and 0.1 mm to 1.5 mm deep, whereby absent an externally applied force, fluid flows from the first capillary region to the second capillary region pursuant to capillary force.

18. An assay device for detecting at least one target ligand in a fluid sample, said assay device comprising:

- a. a sample addition reservoir;
 - b. a time gate for delaying fluid flow;
 - c. a diagnostic element; wherein said assay device is configured and arranged such that said fluid sample flows from said sample addition reservoir to said time gate to said diagnostic element.
19. The assay device of claim 18, wherein said time gate comprises at least one hydrophobic surface.
20. The assay device of claim 18, wherein said time gate comprises hydrophobic poly-electrolytes.
21. The assay device of claim 18, wherein said time gate is V-shaped.
22. The assay device of claim 18, wherein said diagnostic element is clear.
23. The assay device of claim 18, wherein said diagnostic element immobilizes said target ligand for detection.
24. The assay device of claim 18, comprising a used reagent reservoir configured and arranged after said diagnostic element.
25. The assay device of claim 18, wherein said diagnostic element comprises latex particles.
26. The assay device of claim 25, wherein said latex particles have a diameter between 0.01 μm and 10 μm .
27. The assay device of claim 18, wherein said time gate comprises latex particles.
28. The assay device of claim 27, wherein said latex particles have a diameter between 0.01 μm and 10 μm .

29. The assay device of claim 27, wherein said protrusion is 1 nm to 0.5 mm.

30. The assay device of claim 18, wherein said time gate comprises at least one groove.

31. The assay device of claim 30, wherein said groove is parallel to the direction of flow of said fluid sample.

32. The assay device of claim 30, wherein said groove is perpendicular to the direction of flow of said fluid sample.

33. The assay device of claim 18, comprising a reaction chamber configured and arranged between said time gate and said diagnostic element.

34. The assay device of claim 33, wherein said reaction chamber is 0.05 mm to 10 mm deep.

35. The assay device of claim 33, wherein said reaction chamber comprises a ramp.

36. The assay device of claim 35, wherein said ramp is at an angle between 25 degrees and 45 degrees relative to the floor of said reaction chamber.

37. The assay device of claim 18, comprising a sample-reaction barrier configured and arranged between said sample reservoir and said time gate.

38. The assay device of claim 37, wherein said sample-reaction barrier comprises more than one groove between 10 and 500 grooves per centimeter.

39. The assay device of claim 37, wherein said sample-reaction barrier comprises at least one groove.

40. The assay device of claim 39, wherein said groove is perpendicular to the direction of flow of said fluid sample.

41. The assay device of claim 39, wherein said groove is parallel to the direction of flow of said fluid sample.

42. The assay device of claim 39, wherein said groove is 0.01 mm to 0.5 mm deep.

43. The assay device of claim 39, wherein said groove is 0.5 mm to 2 mm wide.

44. The assay device of claim 18, wherein said diagnostic element comprises at least one groove.

45. The assay device of claim 44, wherein said groove is parallel to the direction of flow of said fluid sample.

46. The assay device of claim 44, wherein said groove is perpendicular to the direction of flow of said fluid sample.

47. The assay device of claim 44, wherein said groove is a protrusion.

48. The assay device of claim 44, wherein said groove is spaced between 1 nm and 0.5 mm apart from another groove.

49. The assay device of claim 44, wherein said groove is a depression.

50. The assay device of claim 49, wherein said depression is 1 nm to 0.5 mm.

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TITLE: Diagnostic devices for the
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INVENTOR-INFORMATION:

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422/61 , 422/73 , 422/947

CLAIMS:

I claim:

1. Diagnostic assay device for detecting at least on
target ligand in an
aqueous fluid sample, said device comprising:

i. a sample addition reservoir;

ii. a sample reaction barrier between said sample
addition reservoir and
said reaction chamber;

iii. means for fluid flow from a first capillary in
said sample reaction
barrier (ii) to a second capillary at a reaction chamber
(iv), said first
capillary having a greater capillarity than said second
capillary, and a wall
substantially perpendicular to fluid flow in said first
capillary, said wall
located at the interface between said first capillary and

said second capillary, said means comprising grooves on said wall in said second capillary, said grooves each with an end thereof in contact with fluid flow and being substantially perpendicular to fluid flow, and having widths of between 0.5 mm to 2 mm wide and 0.1 mm to 1.5 mm in depth;

iv. reaction chamber containing at least one conjugate for said target ligand;

v. diagnostic element capable of immobilizing for detecting at least one target ligand in at least one zone;

vi. time gate for delaying fluid flow from said reaction chamber (iv) to said diagnostic element (v) for a preselected time at least sufficient to allow said fluid sample to dissolve said conjugate to form a reaction mixture, said time gate located between said reaction chamber and said diagnostic element, said diagnostic element adapted to receive fluid flow from said reaction chamber through said time gate, said time gate comprising three distinct zones including a first hydrophilic zone, a hydrophobic zone and a second hydrophilic zone, said hydrophobic zone located between said first and second hydrophilic zones, and having a component therein which is capable of binding at least one aqueous soluble component present in said fluid at a rate which changes said hydrophobic zone to a sufficiently hydrophilic surface to delay fluid flow into said second hydrophilic zone, which comprises said diagnostic element (v);

vii. used reagent reservoir.

2. Diagnostic assay device for detecting at least on target ligand in an aqueous fluid sample, said device comprising:

- i. a sample addition reservoir;
- ii. a sample reaction barrier between said sample addition reservoir of said reaction chamber;
- iii. means for fluid flow from a first capillary in said sample reaction barrier (ii) to a second capillary at a reaction chamber (iv), said first capillary having a greater capillarity than said second capillary, and a wall substantially perpendicular to fluid flow in said first capillary, said wall located at the interface between said first capillary and said second capillary, said means comprising grooves on said wall in said second capillary, said grooves each with an end thereof in contact with fluid flow and being substantially perpendicular to fluid flow, and having widths of between 0.5 mm to 2 mm wide and 0.1 mm to 1.5 mm in depth;
- iv. reaction chamber containing at least one conjugate for said target ligand;
- vi. time gate for delaying fluid flow from said reaction chamber (iv) to said diagnostic element (v) for a preselected time at least sufficient to allow said fluid sample to dissolve said conjugate to form a reaction mixture, said time gate located between said reaction chamber and said diagnostic element, said diagnostic element adapted to receive fluid flow from said reaction chamber through said time gate, said time gate comprising three distinct zone including a first hydrophilic zone, a hydrophobic zone and a second hydrophilic zone, said hydrophobic zone located between said first and second hydrophilic zones, and having a component therein which is capable of binding at least one aqueous soluble component present in said fluid at a rate which changes said

hydrophobic zone to a sufficiently hydrophilic surface to delay fluid flow into said second hydrophilic zone, which comprises said diagnostic element (v);

v. diagnostic element capable of immobilizing for detecting at least one conjugate in an amount related to the amount of target ligand in a fluid sample in at least one zone;

vii. used reagent reservoir.

3. Diagnostic assay device for detecting at least one target ligand in an aqueous fluid sample, said device comprising:

i. a sample addition reservoir;

ii. a sample reaction barrier between said sample addition reservoir and said reaction chamber;

iii. means for fluid flow from a first capillary in said sample reaction barrier (ii) to a second capillary at a reaction chamber (iv), said first capillary having a greater capillarity than said second capillary, and a wall substantially perpendicular to fluid flow in said first capillary, said wall located at the interface between said first capillary and said second capillary, said means comprising grooves on said wall in said second capillary, said grooves each with an end thereof in contact with fluid flow and being substantially perpendicular to fluid flow, and having widths of between 0.5 mm to 2 mm wide and 0.1 mm to 1.5 mm in depth;

iv. reaction chamber containing at least one conjugate for said target ligand;

v. diagnostic element capable of immobilizing for detecting at least one target ligand in at least one zone;

vi. time gate for delaying fluid flow from said reaction chamber (iv) to said diagnostic element (vi) for a preselected time at least sufficient to allow said fluid sample to dissolve said conjugate to form a reaction mixture, said time gate located between said reaction chamber and said diagnostic element, said diagnostic element adapted to receive fluid flow from said reaction chamber through said time gate, said time gate comprising three distinct zone including a first hydrophilic zone, a hydrophobic zone and a second hydrophilic zone, said hydrophobic zone located between said first and second hydrophilic zones, and having a component therein which is capable of binding at least one aqueous soluble component present in said fluid at a rate which changes said hydrophobic zone to a sufficiently hydrophilic surface to delay fluid flow into said second hydrophilic zone, which comprises said diagnostic element (v):

vii. means for controlling fluid flow to used reagent reservoir (viii)

viii. used reagent reservoir.

4. Diagnostic assay device for detecting at least one target ligand in an aqueous fluid sample, said device comprising:

i. a sample addition reservoir;

ii. a sample reaction barrier between said sample addition reservoir and said reaction chamber;

iii. means for fluid flow from a first capillary in said sample reaction barrier (ii) to a second capillary at a reaction chamber (iv), said first capillary having a greater capillarity than said second capillary, and a wall

substantially perpendicular to fluid flow in said first capillary, said wall located at the interface between said first capillary and said second capillary, said means comprising grooves on said wall in said second capillary, said grooves each with an end thereof in contact with fluid flow and being substantially perpendicular to fluid flow, and having widths of between 0.5 mm to 2 mm wide and 0.1 mm to 1.5 mm in depth;

iv. reaction chamber containing at least one conjugate for said target ligand;

v. diagnostic element capable of immobilizing for detecting at least one conjugate in an amount related to the amount of target ligand in a fluid sample in at least one zone;

vi. time gate for delaying fluid flow from said reaction chamber (iv) to said diagnostic element (v) for a preselected time at least sufficient to allow said fluid sample to dissolve said conjugate to form a reaction mixture, said time gate located between said reaction chamber and said diagnostic element, said diagnostic element adapted to receive fluid flow from said reaction chamber through said time gate, said time gate comprising three distinct zones including a first hydrophilic zone, a hydrophobic zone and a second hydrophilic zone, said hydrophobic zone located between said first and second hydrophilic zones, and having a component therein which is capable of binding at least one aqueous soluble component present in said fluid at a rate which changes said hydrophobic zone to a sufficiently hydrophilic surface to delay fluid flow into said second hydrophilic zone, which comprises said diagnostic element (v);

vii. means for controlling fluid flow to used reagent

reservoir (viii);

viii. used reagent reservoir.

5. Device of claim 1 or 2 or 3 or 4 optimally having a reagent chamber in fluid contact with said reaction chamber.

6. Device of claim 1 or 2 or 3 or 4 optimally having a reagent chamber in fluid contact with said reaction chamber and said sample addition reservoir.

7. Device of claim 1 or 2 or 3 or 4 wherein at least one signal producing element and at least one receptor capable of combining with said target is contained in said reaction chamber.

8. Device of claim 1 or 2 or 3 or 4 wherein at least one signal producing element and at least one receptor capable of combining with said target is contained on said sample reaction barrier.

9. Device of claim 1 or 2 or 3 or 4 in which said diagnostic element is a grooved surface.

10. Device of claim 1 or 2 or 3 or 4 wherein at least one signal producing element capable of combining with said target is contained in said reaction chamber.

11. Device of claim 1 or 2 or 3 or 4 wherein at least one signal producing element capable of combining with said target is contained on said sample reaction barrier.

12. Diagnostic assay device for detecting a target ligand in a fluid sample, said device comprising:

i. a reaction chamber containing at least one conjugate for said target ligand, and a fluid introducing means for said fluid

sample;

ii. a time gate located between said reaction chamber (i) and said zone (iii) for delaying fluid flow to said zone (iii) for a preselected time at least sufficient to allow said fluid sample to dissolve said conjugate to form a reaction mixture, said time gate comprising three distinct zones including a first hydrophilic zone, a hydrophobic zone and a second hydrophilic zone, said hydrophobic zone located between said first and second hydrophilic zones, and having a component therein which is capable of binding at least one aqueous soluble component present in said fluid at a rate which changes said hydrophobic zone to a sufficiently hydrophilic surface to delay fluid flow into said second hydrophilic zone, which comprises said diagnostic element (vi); and

iii. at least one zone containing at least one immobilized receptor for detecting each desired target ligand.

13. Device of claim 12 in which said zone (iii) is located within a capillary space in said second hydrophilic zone, through which all of said reaction mixture flows.

14. Diagnostic assay device for detecting a target ligand in a fluid sample, said device comprising:

i. a sample addition reservoir;

ii. time gate for delaying fluid flow from said sample addition reservoir (i) to a diagnostic element (iii) for a preselected time, said time gate located between said sample addition reservoir and said diagnostic element, said diagnostic element adapted to receive fluid flow from said reaction

chamber through said time gate, said time gate comprising three distinct zones including a first hydrophilic zone, a hydrophobic zone and a second hydrophilic zone, said hydrophobic zone located between said first and second hydrophilic zones, and having a component therein which is capable of binding at least one aqueous soluble component present in said fluid at a rate which changes said hydrophobic zone to a sufficiently hydrophilic surface to delay fluid flow into said second hydrophilic zone, which comprises said diagnostic element (iii);

iii. diagnostic element capable of receiving fluid flow from said sample addition reservoir, and of immobilizing for detecting at least one conjugate in an amount related to the amount of target ligand in a fluid sample in at least one zone.

15. Device of claim 1, 2, 3, 4 or 14 in which said diagnostic element is located within a capillary space in said second hydrophilic zone, through which all of said reaction mixture flows.

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422/61 , 422/73

CLAIMS:

I claim:

1. Apparatus for blocking for a delay period fluid flow from a first zone to a second zone, said second zone adapted to receive fluid flow from said first zone through a time gate by capillary action, said time gate comprising at least one hydrophobic surface which is capable of binding at least one aqueous soluble component present in said fluid; and whereby the delay period is related to the rate of binding of the aqueous soluble component to said hydrophobic surface which over the delay period changes said hydrophobic surface into a sufficiently hydrophilic surface to allow fluid to flow into said second zone.

2. Apparatus for blocking for a delay period fluid flow

from a first zone
to a second zone, said second zone adapted to receive fluid
flow from said
first zone through a time gate by hydrostatic pressure,
said time gate
comprising at least one hydrophobic surface which is
capable of binding at
least one aqueous soluble component present in said fluid;
and whereby the
delay period is related to the rate of binding of the
aqueous soluble component
to said hydrophobic surface which over the delay period
changes said
hydrophobic surface into a sufficiently hydrophilic surface
to allow fluid to
flow into said second zone.

3. Apparatus of claim 1 or 2 wherein said apparatus is
embedded in a
membrane.

4. Apparatus of claim 1 or 2 in which said component is
a protein, polymer
or detergent.

5. Apparatus of claim 1 or 2 in which said component is
serum albumin.

6. Apparatus of claim 1 or 2 in which said component on
said hydrophobic
surface is latex particles.

7. Apparatus of claim 1 or 2 in which said hydrophobic
surface is composed
of a polyelectrolyte which becomes hydrophilic by exposure
to the buffering
capacity of said fluid and the timed fluid flow is related
to the mass of
polyelectrolyte and the buffering capacity and pH of said
fluid.

8. Apparatus for blocking for a delay period fluid flow
from a first
hydrophilic zone to a second hydrophilic zone, said second
hydrophilic zone
adapted to receive fluid flow from said first zone through
a time gate, said
apparatus comprising three distinct zones, a first

hydrophilic zone, a hydrophobic zone and a second hydrophilic zone, said hydrophobic zone located between said first and second hydrophilic zones, and having a component therein which is capable of binding at least one aqueous soluble component present in said fluid at a rate which over the delay period changes said hydrophobic zone to a sufficiently hydrophilic surface wherein fluid flow is initially blocked from flowing into said second hydrophilic zone and after the delay period the fluid flows into said second hydrophilic zone.

9. Apparatus of claim 8 in which said component is a protein, polymer or detergent.

10. Apparatus of claim 8 in which said component is serum albumin.

11. Apparatus of claim 8 in which said component on said hydrophobic surface is latex particles.

12. Apparatus of claim 8 in which said hydrophobic surface is a polyelectrolyte which becomes hydrophilic by exposure to the buffering capacity of said fluid and the timed fluid flow is related to the mass of polyelectrolyte and the buffering capacity and pH of said fluid.